

What is claimed:

1 1. A method for screening for agents that affect protein degradation rates, the method  
2 comprising:

3 taking a library of cells, the cells expressing a fusion protein comprising a reporter  
4 protein and a protein encoded by a sequence from a cDNA library derived from a sample  
5 of cells, the sequence from the cDNA library varying within the cell library;

6 contacting the library of cells with a plurality of agents which may affect protein  
7 degradation rates;

8 for each agent, selecting cells in the library which express short-lived proteins  
9 based on whether the cells have different reporter signal intensities than other cells in the  
10 library, the difference being indicative of the selected cells expressing shorter lived fusion  
11 proteins than the fusion proteins expressed by the other cells in the library; and

12 characterizing the fusion proteins expressed by the selected cells for each agent.

1 2. A method according to claim 1, wherein the method further comprises comparing  
2 which fusion proteins are expressed by the selected cells for each agent.

1 3. A method for monitoring effects different growth conditions have on expression of  
2 short-lived proteins, the method comprising:

3 exposing samples of cells to different growth conditions;

4 forming cDNA libraries from the sample of cells after exposure to the different  
5 growth conditions;

6 forming a library of cells for each cDNA library, the cells in the library expressing  
7 a fusion protein comprising a reporter protein and a protein encoded by a sequence from  
8 the cDNA library derived from a sample of cells, the sequence from the cDNA library  
9 varying within the cell library;

10 for each library of cells,

11 identifying cells within the library that express fusion proteins that are  
12 degraded *in vivo* more rapidly than other fusion proteins, and

13 characterizing fusion proteins expressed by the identified cells; and

14 comparing which fusion proteins are characterized for each library of cells,  
15 differences in the characterized fusion proteins indicating differences in the short-lived  
16 proteins expressed by when the cells are exposed to the different agents.

1 4. A method according to claim 3, wherein exposing the samples of cells to different  
2 conditions comprises exposing the cells to different agents.

1 5. A method according to claim 3, wherein identifying cells within the library that  
2 express fusion proteins that are degraded *in vivo* more rapidly than other fusion proteins  
3 comprises  
4 modifying a rate of protein expression or degradation by the cells, and  
5 selecting a population of the cells based on whether the cells have different  
6 reporter signal intensities than other cells after the rate of protein expression or  
7 degradation has been modified, the difference being indicative of the selected population  
8 of cells expressing shorter lived fusion proteins than the fusion proteins expressed by the  
9 other cells in the library.

1 6. A method for monitoring effects different growth conditions have on expression of  
2 short-lived proteins, the method comprising:  
3 exposing samples of cells to different conditions;  
4 forming cDNA libraries from the sample of cells after exposure to the different  
5 growth conditions;  
6 forming a library of cells for each cDNA library, each cell in the library expressing  
7 a fusion protein comprising a reporter protein and a protein encoded by a sequence from  
8 the cDNA library derived from a sample of cells, the sequence from the cDNA library  
9 varying within the cell library;  
10 for each library of cells,  
11 partitioning the library of cells into populations of cells based on an  
12 intensity of a reporter signal from the fusion protein such that cells partitioned into  
13 a given population have a reporter signal within a desired range of reporter signal  
14 intensity,

15                   modifying a rate of protein expression or degradation by the cells for a  
 16                   given population of cells,  
 17                   selecting a subpopulation of the cells from the given population of cells  
 18                   based on whether the cells have a different reporter signal intensity than the other cells in  
 19                   the given population, the difference being indicative of the selected subpopulation of cells  
 20                   expressing shorter lived fusion proteins than the fusion proteins expressed by the other  
 21                   cells in the given population  
 22                   characterizing fusion proteins expressed by at least a portion of the selected  
 23                   cells; and  
 24                   comparing which fusion proteins are characterized for each library of cells,  
 25                   differences in the characterized fusion proteins indicating differences in the short-lived  
 26                   proteins expressed by when the cells are exposed to the different agents.

1       7.       A method according to claim 6 wherein exposing the samples of cells to different  
 2       conditions comprises exposing the cells to different agents.

1       8.       A method for screening for differences in short-lived proteins expressed by first  
 2       and second cell samples, the method comprising:  
 3                   forming cDNA libraries for first and second samples of cells;  
 4                   forming a library of cells for each cDNA library, the cells in the library expressing  
 5       a fusion protein comprising a reporter protein and a protein encoded by a sequence from  
 6       the cDNA library derived from a sample of cells, the sequence from the cDNA library  
 7       varying within the cell library;  
 8                   for each library of cells,  
 9                   identifying cells within the library that express fusion proteins that are  
 10                  degraded *in vivo* more rapidly than other fusion proteins, and  
 11                  characterizing fusion proteins expressed by the identified cells; and  
 12                  comparing which fusion proteins are characterized for each library of cells,  
 13       differences in the characterized fusion proteins indicating differences in the short-lived  
 14       proteins expressed by the first and second samples cells.

1 9. A method for screening for differences in short-lived proteins expressed by first  
2 and second cell samples, the method comprising:  
3 forming cDNA libraries for first and second samples of cells;  
4 forming a library of cells for each cDNA library, the cells in the library expressing  
5 a fusion protein comprising a reporter protein and a protein encoded by a sequence from  
6 the cDNA library derived from a sample of cells, the sequence from the cDNA library  
7 varying within the cell library;  
8 for each library of cells,  
9 partitioning the library of cells into populations of cells based on an  
10 intensity of a reporter signal from the fusion protein such that cells partitioned into  
11 a given population have a reporter signal within a desired range of reporter signal  
12 intensity,  
13 modifying a rate of protein expression or degradation by the cells for a  
14 given population of cells,  
15 selecting a subpopulation of the cells based on whether the cells have  
16 different reporter signal intensities than the other cells after the rate of protein expression  
17 or degradation has been modified, the difference being indicative of the selected  
18 subpopulation of cells expressing shorter lived fusion proteins than the fusion proteins  
19 expressed by the other cells in the given population, and  
20 characterizing fusion proteins expressed by at least a portion of the selected  
21 cells; and  
22 comparing which fusion proteins are characterized for each library of cells,  
23 differences in the characterized fusion proteins indicating differences in the short-lived  
24 proteins expressed by the first and second samples cells.